Journal of Surgical Oncology 64:336–340 (1997)

Multiple Lymphomatous Polyposis

ABDURRAHMAN KADAYIFÇI, MD, MUSTAFA BENEKLI, MD,[1]* M. CEMİL SAVAŞ, MD,[1]
SERAP ARSLAN, MD,[1] BEDRİ UZUNALİMOĞLU, MD,[2] İBRAHİM BARIŞTA, MD,[1]
İBRAHİM H. GÜLLÜ, MD,[1] AND GÜLTEN TEKUZMAN, MD[1]
[1]*Department of Internal Medicine, Hacettepe University Faculty of Medicine, Ankara, Turkey*
[2]*Department of Pathology, Hacettepe University Faculty of Medicine, Ankara, Turkey*

Multiple lymphomatous polyposis (MLP) is a distinctive and particularly rare clinical type of malignant gastrointestinal lymphoma, which is classified as B-cell centrocytic non-Hodgkin's lymphoma. This rare entity has been recently reclassified as mantle cell lymphoma. We herein report three additional cases of MLP involving various segments of the gastrointestinal tract. MLP has an aggressive biologic behavior and a relatively poor prognosis and must be treated accordingly as a high-grade lymphoma with systemic chemotherapy. *J. Surg. Oncol. 64:336–340, 1997.*

KEY WORDS: multiple lymphomatous polyposis; non-Hodgkin's lymphoma; gastrointestinal tract

INTRODUCTION: A RARE CLINICAL TYPE

Multiple lymphomatous polyposis (MLP) is an unusual presentation of malignant gastrointestinal (GI) lymphomas characterized by the formation of multiple polyps along the GI tract [1]. We present three new cases of MLP with radiologic, endoscopic, and histopathologic features. The involvement was limited to the colon and rectum in the first patient, whereas the bulbus of the duodenum was also involved together with the colon and rectum in the second case. The third patient had MLP throughout the entire GI tract.

CASE REPORTS

Case 1

A 70-year-old man was admitted in April 1994 with the complaints of constipation, rectal bleeding, and a 10-kg weight loss over the previous 3 months. There were multiple cervical, supraclavicular, axillary, and inguinal lymphadenopathies in various sizes. The liver was palpable 6 cm below the left costal margin. Laboratory data showed a hemoglobin of 9.4 g/dl and a white blood cell count of 11.4×10^9/l with a normal differential. Erythrocyte sedimentation rate (ESR) was 82 mm/h. Renal and hepatic function tests were normal. There were bilateral hilar lymphadenopathies on chest X-ray. A barium enema of the colon showed multiple polypoid defects most prominent in the rectum and sigmoid colon (Fig. 1). Colonoscopy demonstrated multiple polypoid lesions that macroscopically resembled polyposis coli of the colon and rectum (Fig. 2). Histopathological examination of the polyps revealed diffuse, small-cleaved, cell type non-Hodgkin's lymphoma (Fig. 3). Upper endoscopy and small bowel barium enema examination showed no further lesion. A computerized tomography (CT) of abdomen demonstrated multiple paraaortic and paracaval lymph nodes. Bone marrow biopsy showed nodular lymphocytic infiltration. Systemic chemotherapy with cyclophosphamide-Adriamycin-vincristine-prednisolone (CHOP) regimen was initiated, but the patient died at the third month of the treatment.

Case 2

A 55-year-old woman was admitted in July 1995 with the complaint of fatigue during the last 6 months. Physical examination was unremarkable except for an apparent paleness. A severe anemia (Hb: 8.1 g/dl) and occult blood positivity in the stool were detected in initial laboratory tests. ESR was 60 mm/h. A rectosigmoidoscopic examination revealed diffuse polypoid lesions in different sizes along the lumen. The mucosa of the colon between polyps was normal in appearance. A double-contrast barium enema of the colon (Fig. 4) and colonos-

*Correspondence to: Mustafa Benekli, MD, 14. Sokak. 43/3, Bahçelievler, Ankara, Turkey. Fax: 90-312-3242009.
Accepted for publication 10 December 1996

Fig. 1. Barium enema examination of the colon showing multiple polypoid nodules.

copy showed that these polyps were present in all segments of the colon up to the ileocecal valve. An upper endoscopy showed the same lesions only in the duodenal bulbus (Fig. 5). The other parts of the duodenum and stomach were not involved. The barium enema study of the small intestine was also normal. Biopsies obtained from different sites of the colon and the bulbus of the duodenum showed diffuse, small-cleaved, cell type non-Hodgkin's lymphoma (Fig. 6A, B). There was no lymph node enlargement in abdominal CT. No evidence of liver, spleen, and bone marrow involvement was found in the systematic screening for malignant lymphoma. She was started on CHOP chemotherapy and received five courses of CHOP regimen until her last visit in February 1996 with no evident response.

Case 3

A 54-year-old man presented with nausea, vomiting, constipation, and rectal bleeding in November 1990. On physical examination, he had no palpable peripheral lymph nodes. The liver was palpable ~3 cm on the right costal margin. Laboratory investigations were normal except for a mild anemia (Hb: 10.9 g/dl). Barium enema series and upper and lower endoscopic examinations revealed multiple polypoid structures throughout the entire

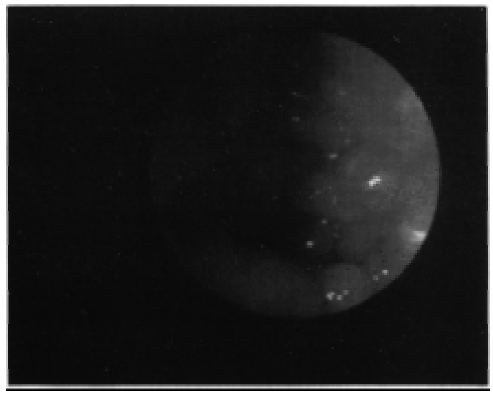

Fig. 2. Colonoscopic view of lymphomatous polyps in descending colon.

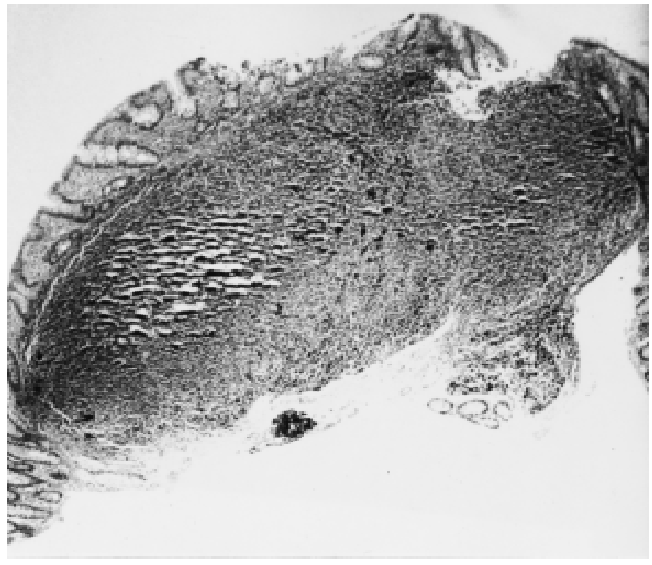

Fig. 3. Diffuse lymphoma growth in the submucosa partly covered by intact, compressed colonic mucosa. Defects in the mucosa represents technical artefacts (H&E; ×115).

GI tract. A histopathological diagnosis of non-Hodgkin's lymphoma, diffuse, small-cleaved, cell type was established. The patient was given six courses of CHOP regimen with limited success. Later, he received mesna-ifosfamide-etoposide (MIE) and cyclophosphamide-vincristine-methotrexate-leucovorin-cytosine arabinoside (COMLA) regimens, respectively, for salvage therapy. In May 1994, the patient was readmitted with the complaints of dysphagia and dyspnea and found to have a right-sided tonsillary mass obstructing the upper airway, which on biopsy revealed diffuse, large cell type, malignant lymphoma. He was started on oral prednisolone-etoposide-chlorambucil-CCNU (PECC) regimen for resistant disease. However, the patient's condition progres-

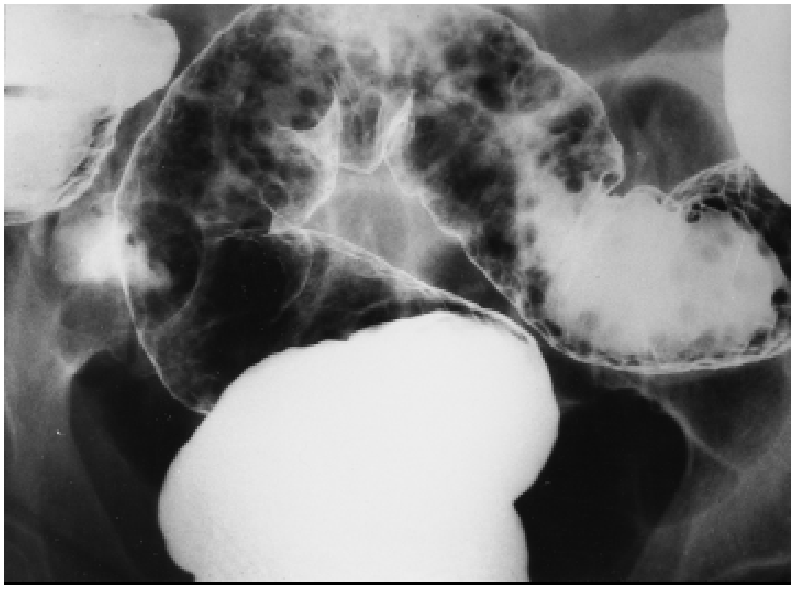

Fig. 4. Double-contrast enema of colon with numerous lymphomatous polyps.

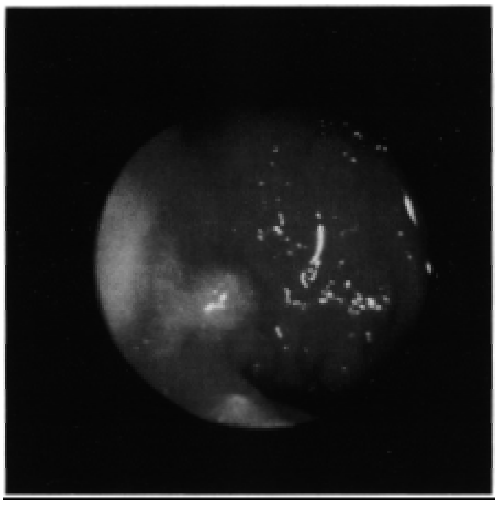

Fig. 5. Endoscopic photograph of the duodenal bulbus showing small polypoid lesions.

sively deteriorated and he died of progressive disease 4 weeks after the admission.

DISCUSSION

The GI tract is the most common site of primary extranodal lymphomas and is involved in nearly 20–30% of all malignant lymphomas [2–4]. However, GI lymphomas comprise only 1–4% of all GI malignancies [4,5]. Malignant lymphomas of the alimentary tract appear in four types: (1) annular or plaque-like lesions, (2) aneurysmal lesions, (3) bulky protuberant growths, and (4) MLP [6]. MLP is the least common type of primary intestinal lymphomas, accounting for 1–2% of cases.

The term ''multiple lymphomatous polyposis'' was first presented by Cornes in 1961 to describe numerous polypoid lesions throughout the entire GI tract consisting of mucosal involvement by malignant lymphoma [1]. In 1980, Blackshaw classified MLP as B-cell centrocytic non-Hodgkin's lymphoma according to the Kiel classification [7,8]. According to the Working Formulation, MLP is classified as a diffuse, small-cleaved cell malignant lymphoma [9]. Isaacson et al. [10] and Triozzi et al. [11] have suggested that MLP is the digestive counterpart of mantle zone lymphoma that arises in lymph nodes.

A literature review was performed by a search of the Medline using Dialog onDisc® between 1966–1995. MLP was usually described as isolated case reports or documentation of small series. Because the cases reported before 1971 represented a heterogenous group of lymphomas, they are ignored. In 1994, Mynster et al. [12] reviewed 31 cases in detail since 1971 and described one additional case of their own. We uncovered a further 43 cases of MLP described in the literature after their report, reaching a total of 78 patients, including our three cases. The chief symptoms at presentation were weight loss, weakness, diarrhea, abdominal pain, rectal bleeding, and anemia. There was a remarkable male predominance. Extradigestive dissemination was noted in the majority of the patients. Chemotherapy was the most preferred treatment modality, but usually with a dire prognosis. Mean survival was generally <3 years.

Our patients showed typical features of MLP described in large series [12,13]. The involvement was limited to the colon and rectum in the first patient and the size of the polyps varied between 0.5–2 cm. Only the bulbus of the duodenum showed polypoid lesions in ad-

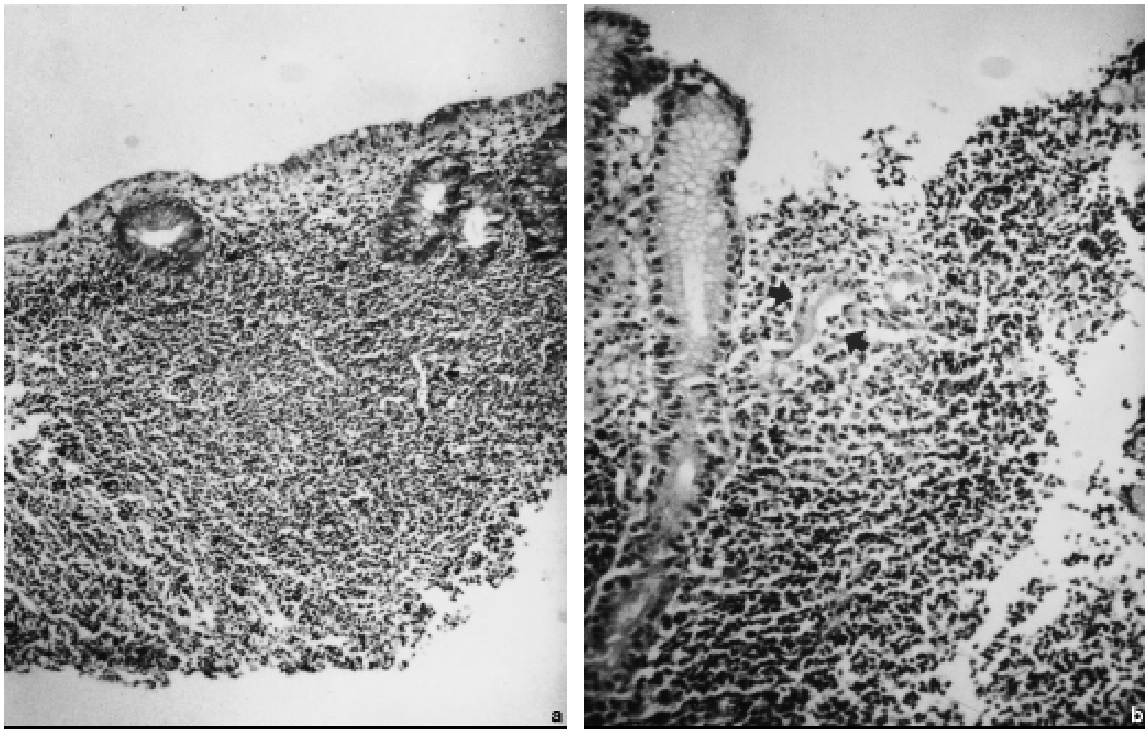

Fig. 6. **A:** Colonoscopic biopsy specimen from the second patient showing lymphoma in the mucosa. Only superficial crypts are preserved (H&E; ×230). **B:** Gastric mucosa from the same patient. Diffuse lymphocytic lymphoma infiltration in the lamina propria, arrows show a lymphoepithelial region destruction of a foveolar gland by atypical lymphoid infiltration. The long glandular structure represents a relatively intact foveolar gland (H&E; ×230).

dition to the colon and rectum in the second patient. The endoscopic appearance of these polyps was similar to colonic polyps and histopathologic examination showed the same findings in both the duodenal and colonic biopsies. Entire gut was involved in the third patient. MLP cases with a widespread distribution from stomach to rectum have been reported before [14]. However, selective duodenal bulbus involvement together with colon and rectum has not been reported previously. Recently, Pals et al. [15] showed the specific expression of the mucosal homing receptor $\alpha 4\beta 7$ in MLP, which mediates lymphocytic sedimentation to the GI mucosa by binding to a mucosal adhesion molecule named mucosal vascular adressin (MAdCAM-1). The involvement of separate intestinal segments at the time of presentation in our patient also supports the possible role of a tissue-specific homing mechanism for lymphoma cells via adhesion molecules.

The secondary transformation of MLP to large cell lymphoma is extremely uncommon and has been described previously only in two patients [12,16]. High-grade lymphoma was said to be present in regional nodes and in extradigestive locations rather than the GI tract itself. In our patient, large cell lymphoma was located in the tonsils in accordance with these reports. The association of MLP with large cell lymphoma might also simply be incidental, but this does not seem likely.

Extraintestinal spread of MLP is frequently found at the time of diagnosis. The survival rate of these patients is not high despite intensive chemotherapy [12,13,17]. Median survival is ~24–36 months. Generalised lymphadenopathy, hepatomegaly, and bone marrow involvement were present in our first case at the diagnosis, and the patient died 3 months after the beginning of the therapy. However, our third patient lived 43 months. Because the prognosis is poor, MLP should be considered as a high grade lymphoma and treated accordingly with chemotherapy [12]. Autologous stem cell transplantation following high dose radiochemotherapy was applied recently in four patients with MLP with a considerable success [17]. Surgical therapy is not recommended in MLP because of widespread localization and frequent extradigestive involvement. However, surgery is indicated only in patients with complications such as obstruction, perforation and severe bleeding.

The differential diagnosis of benign and malignant polypoid neoplasia of the GI tract is extremely important because of the poor prognosis. The clinical, radiological, and endoscopic findings of polypoid lesions, lymphoid or epithelial in orgin, may be quite similar, and histopathological intervention is required for definitive diagnosis and evaluation of prognosis. It is important to differentiate the MLP from benign and malignant polypoid diseases of the GI tract as it requires different management

strategies. MLP should be kept in mind during the evaluation of multiple polyps of the GI tract.

REFERENCES

1. Cornes JS: Multiple lymphomatous polyposis of the gastrointestinal tract. Cancer 1961;14:249–257.
2. Barişta I, Tekuzman G, Firat D, et al.: Non-Hodgkin's lymphomas in Turkey: Eighteen years' experience at the Hacettepe University. Jpn J Cancer Res 1994;85:1200–1207.
3. Freeman C, Berg JW, Cutler SJ: Occurrence and prognosis of extranodal lymphomas. Cancer 1972;29:252–260.
4. Lewin KJ, Ranchod M, Dorfman RF: Lymphomas of the gastrointestinal tract: A study of 117 cases presenting with gastrointestinal disease. Cancer 1978;42:693–707.
5. Loehr WS, Mujahed Z, Zahn DF, et al.: Primary lymphoma of the gastrointestinal tract: a review of 100 cases. Ann Surg 1969;170: 232–238.
6. Dawson IMP, Cornes JS, Morson BC: Primary malignant tumours of the intestinal tract. Br J Surg 1961;49:80–89.
7. Blackshaw AJ: Non-Hodgkin's lymphomas of the gut. In Wright R (ed): ''Recent Advances in Gastrointestinal Pathology.'' Eastbourne, UK: WB Saunders, 1980, p 213–240.
8. Stansfeld AG, Diebold J, Kapanci Y, et al.: Updated Kiel classification for lymphomas. Lancet 1988;1:292–293.
9. The Non-Hodgkin's Lymphoma Pathologic Classification Project: National Cancer Institute sponsored study of classifications on Non-Hodgkin's lymphomas: Summary and description of a working formulation for clinical usage. Cancer 1982;49:2112–2135.
10. Isaacson PG, MacLennan KA, Subbuswamy SG: Multiple lymphomatous polyposis of the gastrointestinal tract. Histopathology 1984;8:641–656.
11. Triozzi PL, Borowitz MJ, Gockerman JP: Gastrointestinal involvement and multiple lymphomatous polyposis in mantle zone lymphoma. J Clin Oncol 1986;4:866–873.
12. Mynster T, Hultberg B, Bülow S: Multiple lymphomatous polyposis of the colon and rectum: Report of a case and review of the literature. Scand J Gastroenterol 1994;29:545–549.
13. Lavergne A, Brouland JP, Launay E, et al.: Multiple lymphomatous polyposis of the gastrointestinal tract. An extensive histopathologic and immunohistochemical study of 12 cases. Cancer 1994;74:3042–3050.
14. Smir BN, Pulitzer DR: Multiple lymphomatous polyposis of the gut: A case with unusually widespread distribution. J Clin Gastroenterol 1994;19:139–142.
15. Pals ST, Drillenburg P, Dragosics B, et al.: Expression of the mucosal homing receptor $\alpha 4\beta 7$ in malignant lymphomatous polyposis of the intestine. Gastroenterology 1994;107:1519–1523.
16. Harris M, Blewitt RW, Davies VJ, Steward WP: High-grade non-Hodgkin's lymphoma complicating polypoid nodular lymphoid hyperplasia and multiple lymphomatous polyposis of the intestine. Histopathology 1989;15:339–350.
17. Mahé B, Moreau A, Moreau P, et al.: High dose radiochemotherapy followed by autologous stem cell transplantation in four patients with multiple lymphomatous polyposis. Cancer 1995;75: 2742–2746.